This factsheet is about natalizumab, a disease modifying therapy (DMT) for relapsing multiple sclerosis (MS). At the end of this factsheet you’ll find out where you can get more information on this drug, other drugs for MS and the benefits of early treatment.

What is natalizumab?
Natalizumab is a drug that was given a licence in the UK to be used against ‘highly active’ relapsing MS in 2006. In 2007 it was given the go ahead for use on the NHS by the National Institute for Health and Care Excellence (NICE). It was the first monoclonal antibody approved to treat MS (the reason its name ends with ‘mab’).

Natalizumab is pronounced: nata-LEE-zoo-mab.
Its brand name is Tysabri (ty-SAB-ree).

Can I have this drug?
Natalizumab is recommended for the treatment of relapsing MS that is ‘highly active’ or severe and getting worse fast. This means - whether you’re on a DMT already or not - you’re getting frequent relapses and there are signs on MRI scans that your MS is active. These signs include new ‘lesions’ (areas of damage) in your brain.

In some circumstances natalizumab might be the first DMT someone is given. But because it can have serious side effects it’s usually given after another DMT hasn’t worked well enough.

So you can take natalizumab if you have:

- relapsing MS and you’ve had a relapse in the last year and MRI scans show new signs that your MS is active (you have new ‘lesions’). This is despite taking another DMT
- relapsing MS and you’ve had at least two relapses in the last year and MRI scans show new signs that your MS is active. This is happening whether or not you’ve been taking another DMT

Whether you’ll be offered this drug depends on if you qualify for it based on guidelines used by your MS specialist. These come from the Association of British Neurologists (ABN) and NICE. It also depends on whether the NHS where you live will pay for it. NHS guidelines on this tend to follow what NICE says.

You won’t get this drug if:

- you’re already on another DMT that’s controlling your MS well. You can’t take more than one DMT at a time
- your MS isn’t ‘highly active’ or severe and getting worse fast
- you have progressive MS

Natalizumab won’t work if your MS doesn’t have relapses, so you won’t be offered it if you have primary progressive MS. A trial in 2015 showed it doesn’t work if you have secondary progressive MS either. But several other drugs are now being tested to see if they work for people with these non-relapsing, progressive types of MS.

You might not be able to take this drug if you have some health conditions. So tell your MS specialist your full medical history, including any other health problems and medications you’re taking.
If you're a woman trying to have a baby, or not using contraception, you should discuss with your MS specialist the possible risk this drug might pose to your baby if you become pregnant (see the section What side effects might I get?).

**How do I take it?**

Natalizumab is given through a drip (an ‘infusion’) in hospital. This takes about an hour, with another hour for you to be monitored. You need to go to hospital once every four weeks for your infusion, but you don’t need to stay overnight.

During each infusion, natalizumab is slowly pumped into your bloodstream through a needle that goes into a vein, usually in your arm. You normally sit in a chair or lie on a bed during an infusion.

**How does it work?**

Your immune system fights off infections. But with MS it attacks the nerves in your brain and spinal cord by mistake. This leads to inflammation and damage, especially to the coating that covers your nerves (myelin). This damage interferes with how signals travel along these nerves. Over time this affects your control over many parts of your body and causes symptoms of MS.

Natalizumab reduces this damage by targeting special types of immune cells known as white blood cells or ‘lymphocytes’, especially ones called T cells. These are thought to be responsible for much of the damage caused in relapsing MS.

Your immune system protects you from disease by making antibodies that attach themselves to viruses and bacteria and destroy them. Natalizumab is a man-made (‘monoclonal’) antibody that’s been designed to stick to your T cells and kill them. This stops them before they enter your brain and spinal cord where they would attack the protective myelin coating around your nerves.

**How well does it work?**

When DMTs, including natalizumab, are working well you have:
- fewer and less serious relapses
- fewer new or bigger ‘lesions’ (or ‘plaques’) in your brain and spinal cord (lesions can be seen on MRI scans)
- a slowdown in your disability getting worse

Like other DMTs, natalizumab works best the sooner you start it after you’re diagnosed with MS. Taking it later can also have benefits but it can’t undo any permanent disability you may already have.

DMTs can be split into three groups, according to how big their effect can be.

**High (they can work very well):**
- alemtuzumab (Lemtrada)
- natalizumab (Tysabri)

**Good (they can work well):**
- dimethyl fumarate (Tecfidera)
- fingolimod (Gilenya)

**Moderate (they can work fairly well):**
- glatiramer acetate (Copaxone)
- five different beta interferons (Avonex, Betaferon, Extavia, Rebif and Plegridy)
- teriflunomide (Aubagio)
The effectiveness of natalizumab is classed as 'high'

Relapses dropped by: 68%
This means that in a trial, on average, people saw a 68% drop in the number of relapses they had. This was compared to people who took a placebo, a dummy treatment with no drug in it.

How many people stayed free of relapses when they took this drug?

67% of people who took natalizumab stayed free of relapses over two years.

![Diagram showing 67% of people stayed free of relapses](image1)

41% of people who took the placebo stayed free of relapses.

![Diagram showing 41% of people stayed free of relapses](image2)

Disability getting worse was slowed down by: 42%
This means that in a trial, on average, people saw a 42% drop in the risk of their disability getting worse. This was compared to people who took a placebo.

How many people’s disability didn’t get worse when they took this drug?

Disability didn’t get worse over two years for 83% of people who took natalizumab.

![Diagram showing 83% of people’s disability didn’t get worse](image3)

Disability didn’t get worse for 71% of people on the placebo.

![Diagram showing 71% of people’s disability didn’t get worse](image4)

The evidence about the benefits of natalizumab here comes from a trial called AFFIRM. A total of 942 people took part over two years.

Natalizumab might work much better for you than these average results - or it might not work as well. **Long-term benefits**: studies are underway looking at this drug’s longer term benefits. Evidence shows that it’s still working after five years with no new risks that we didn’t already know about.
What side effects might I get?

Like all drugs, natalizumab can have side effects, but not everyone gets them. Not many people stop taking this drug because of side effects.

The more effective a DMT is, the more risk of serious side effects. Natalizumab is, along with alemtuzumab, the DMT that controls MS best but with the biggest risk of serious side effects.

Natalizumab lowers the number of cells in your immune system. This leaves you more likely to get infections. The drug doesn’t target all types of your immune cells, so it still leaves you with enough protection against infections.

It’s not yet known for certain if natalizumab can seriously harm unborn babies. So far studies of pregnant women suggest it doesn’t. If you’re a woman who might get pregnant discuss this with your MS specialist. You may be advised to use reliable contraception (eg, the ‘pill’ or condoms) while you take this drug. This is also true for up to three months after you stop taking natalizumab.

Your MS specialist, GP or MS nurse can give you advice about ways of dealing with side effects.

The most common side effects
(up to one in ten people get them)

**Infusion reactions** – these last an hour or so and can include:
- hives (an itchy skin rash)
- shivering
- feeling sick or dizzy
- headache
- pain in your joints
- tiredness

Other common side effects, which may affect up to one in ten people, include infections of your urinary tract, lungs, nose and throat. You might also get pain in your arms, legs and stomach, diarrhoea or depression.

More serious side effects

A small minority of people have a more serious allergic reaction with:
- hives (an itchy skin rash)
- swelling of your face, lips or tongue
- difficulty breathing
- chest pain
- fever
- feeling flushed (your face and chest go red)

This happens to about one in 25 people. One in a hundred get an even more severe allergic reaction.

Serious infections

Natalizumab leaves you more open to infections, some of which might be serious such as meningitis (inflammation of the brain). Get medical help straight away if you notice any of the following:
- fever
- stiff neck
- headache
- severe diarrhoea
- shortness of breath
- dizziness that lasts a long time
- weight loss
- lack of energy or enthusiasm

Liver problems

- symptoms include your skin or the whites of your eyes going yellow and your urine going dark

More information and support

You’ll find where you can get a full list of all possible side effects and other information about this drug.
PML: a serious side effect

Natalizumab can increase your chances of getting a brain infection called PML (progressive multifocal leukoencephalopathy). PML often leaves people seriously disabled or kills them. Up to one in four people with PML die from it.

PML is caused by the JC virus. Over half of people with MS have this virus. Our immune system normally stops it causing us problems but natalizumab changes the immune system, allowing this virus to become active. You’re at even higher risk of PML if you’ve ever used a drug that suppresses your immune system like mitoxantrone (but if you’ve used DMTs like beta interferon or glatiramer acetate that doesn’t increase your risk).

You’re at the highest risk of PML if these three things are all true for you:
1. you have the JC virus
2. you take natalizumab for longer than two years
3. you previously used a drug that suppressed your immune system

Around four in every thousand people who take this drug get PML. Only one in 10,000 people who don’t have JC virus get it. But in people who do have the virus around one in 500 of those at the highest risk get PML in the first two years of taking natalizumab. After two years the risk in people with JC virus goes up a lot. An estimate in 2016 put the risk of PML much higher in people with JC virus. People with all three risk factors mentioned earlier could have a one in 44 chance of getting PML.

By November 2015 around 600 people taking natalizumab had developed PML (out of over 140,000 people across the world taking this drug).

A blood test will show if you have the JC virus. If you do have it, your health care team will talk to you about changing your treatment (leaving a longer time between doses or switching to a different drug). You might have a test that shows you don’t have this virus then a later tests finds it. That’s because you’ve become infected since the earlier test.

For this reason everyone taking natalizumab is tested regularly and checked for early signs of PML. Even if you stop taking the drug you should look out for possible PML symptoms for the next six months. Signs of PML are similar to an MS relapse: clumsiness, weakness on one side and changes in your speech, vision or memory and thinking.

This last point has recently become clearer. We now know that damage could be taking place in your brain between relapses, when it might seem nothing is happening with your MS. Before deciding, talk to others and get the information you need. Some ideas are in the section More information and support.

What tests will I need?

Before you start this drug you’ll have an MRI scan of your brain. You’ll have more scans early on in your treatment, then one at least once a year to see how the drug is controlling your MS.
Before you take natalizumab you should have a blood test for the JC virus. If you have this virus, your MS specialist will talk to you about the risk this puts you at of the brain infection PML if you take this drug. If you decide to take it you’ll be monitored for signs of PML. This includes MRI scans every three to six months if you’re at high risk for PML. If you don’t have the JC virus, you’ll be tested every six months to see if you’ve picked it up since starting natalizumab.

You’ll also have blood tests that check your liver and see if you’ve developed neutralising antibodies that can stop natalizumab working (see the box on the next page about neutralising antibodies).

**When should I stop taking this drug?**

Natalizumab, like all DMTs except one, is meant to be taken long term. Some people have been taking natalizumab for almost a decade. Two trials are following people on this drug for over ten years. If natalizumab is controlling your MS well and side effects aren’t a problem you should be able to take it for years.

Your specialist might recommend you stop taking natalizumab and switch to another DMT. This can happen if you have bad side effects or the drug isn’t controlling your MS. Switching drugs usually only happens after you’ve taken a drug for six months. But if you have the JC virus you may be taken off the drug after two years and put on another DMT (usually fingolimod). This is because after two years your risk of getting the brain infection PML goes up a lot.

**You’ll need to stop taking natalizumab if:**

- there are signs that you have developed PML or your specialist feels the chances of this are too high
- you develop a serious infection. Your MS specialist might decide that it’s best to stop taking natalizumab for a while
- you develop neutralising antibodies (see box on next page)
- your MS changes to secondary progressive MS. DMTs available now can’t help people with progressive MS if they don’t have relapses. But clinical trials are underway testing drugs for people with progressive, non-relapsing types of MS.

You’ll also need to discuss with your MS specialist whether to stop taking natalizumab if you’re a woman thinking about getting pregnant.

(see next section for more details).

**I want a child. Can I take natalizumab?**

We don’t know yet for sure which DMTs are totally safe to take when pregnant. This includes natalizumab. Studies so far of women who have taken natalizumab when pregnant seem to show it doesn’t cause serious harm to unborn babies. All the same you should discuss with your specialist if:

- you’re a woman trying to get pregnant
- you’re already pregnant (or think you might be)
- you want to breastfeed

You and your MS specialist will weigh up the potential risk of the drug affecting your baby against the risk of stopping the drug and your MS getting worse. Women on this drug who get pregnant sometimes carry on taking it if their MS has been very active.

If you’re a woman trying for a baby and you decide to stop taking this drug, you need to wait until the amount of it in your body drops to a safe level. The time this takes is called the ‘washout period’. For natalizumab it’s up to three months. Blood tests will check that the level of drug in your blood has dropped low enough.

Women who’ve just had a baby are more likely to have a relapse. So it’s recommended they restart their DMT soon after giving birth. But if you’re a mother who wants to breastfeed you shouldn’t feed this way while taking natalizumab (or up to three months after your last infusion). This is because the drug gets into breast milk and it’s not known if this could harm your baby.

Men and women with MS who would like to have a child should discuss this with their MS specialist. Women who think they may be pregnant should also talk to their MS specialist.
Neutralising antibodies

Your immune system makes antibodies to kill viruses and bacteria. Some people find their body makes ‘neutralising antibodies’ against some MS drugs. Over time these antibodies can stop the drug working. Regular blood tests will pick this up. You’ll then switch to a new DMT.

The chances of developing these antibodies to natalizumab are different depending on how long you take the drug. In one study tests showed this was a problem for around 6% of people taking natalizumab.

More information and support

www.mssociety.org.uk/earlytreatment

On this web page you’ll find more about treatment, a report on the evidence for early treatment and links to our basic guide to DMTs and factsheets on other DMTs.

New guidelines say everyone should have a review of their MS and treatment with a specialist at least once a year. But if you’re not happy with the treatment you’re offered, find tips about what to do in our Talking about treatments checklist, also on this link.

Elsewhere on the MS Society site you’ll find the latest updates on research into drugs for the different types of MS.

Patient information leaflets

Every DMT comes with detailed information about doses, how to store and take it, side effects and results from trials. Find the one for this drug at www.medicines.org.uk and search for ‘natalizumab’ or ‘Tysabri’. The circle with ‘PIL’ on it has information written for patients. The circle with ‘SPC’ on it has information for doctors.

Your MS specialist team

Your neurologist, MS nurse and other members of your specialist team can give you information and support, as can your GP often. MS nurses, if you have one where you are, can be especially helpful if you need support taking a DMT.

www.mssociety.org.uk/forum

On this and other online forums you can talk to others thinking about treatment or already taking it.
About this resource
With thanks to Louise Coghlin and all the neurologists and people with MS who contributed to this factsheet.

Disclaimer: We have made every effort to ensure that the information in this publication is correct. We do not accept liability for any errors or omissions. Availability and prescribing criteria for drugs in various parts of the UK may change. Be sure to seek local advice from the sources listed.

Let us know what you think
If you have any comments on this information or on the work of the MS Society, please send them to resources@mssociety.org.uk, or you can complete our short online survey at www.surveymonkey.com/s/MSresources

DMT factsheet: natalizumab (Tysabri)

References
A list of references is available on request, and all cited articles are available to borrow from the MS Society library (there may be a small charge). Contact the librarian on 020 8438 0900, or visit www.mssociety.org.uk/library

Further information from the MS Society

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Helpline
The Freephone MS Helpline offers confidential emotional support and information for anyone affected by MS, including family, friends and carers.

Information is available in over 150 languages through an interpreter service.

☎ 0808 800 8000 (weekdays 9am–9pm)
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Together, we are strong enough to stop MS.

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